```
JUL 2 3 2002
                                SEQUENCE LISTING
<110> RAPPUOLI, RICERADEN
      GRANDI, Guido
<120> POLYEPITOPE CARRIER PROTEIN
<130> PP00362.102 / 2302-0362
<140> 09/674,183
<141> 2000-11-14
<150> PCT/IB99/00844
<151> 1999-04-27
<150> GB9808932.9
<151> 1998-04-27
<160> 20
<170> PatentIn Ver. 2.1
<210> 1
<211> 15
<212> PRT
<213> T-cell epitope P23TT
<400> 1
Val Ser Ile Asp Lys Phe Arg Ile Phe Cys Lys Ala Asn Pro Lys
                                      10
<210> 2
<211> 16
<212> PRT
<213> T-cell epitope P32TT
<400> 2
Leu Lys Phe Ile Ile Lys Arg Tyr Thr Pro Asn Asn Glu Ile Asp Ser
<210> 3
<211> 16
<212> PRT
<213> T-cell epitope P21TT
<400> 3
```

Ile Arg Glu Asp Asn Asn Ile Thr Leu Lys Leu Asp Arg Cys Asn Asn

TECH CENTER 1600/2900

<210> 4 <211> 18

```
<212> PRT
<213> T-cell epitope PF T3
<400> 4
Glu Lys Lys Ile Ala Lys Met Glu Lys Ala Ser Ser Val Phe Asn Val
Val Asn
<210> 5
<211> 21
<212> PRT
<213> T-cell epitope P30TT
<400> 5
Phe Asn Asn Phe Thr Val Ser Phe Trp Leu Arg Val Pro Lys Val Ser
                                      10
Ala Ser His Leu Glu
             20
<210> 6
<211> 14
<212> PRT
<213> T-cell epitope P2TT
<400> 6
Gln Tyr Ile Lys Ala Asn Ser Lys Phe Ile Gly Ile Thr Glu
<210> 7
<211> 13
<212> PRT
<213> T-cell epitope HA
<400> 7
Pro Lys Tyr Val Lys Gln Asn Thr Leu Lys Leu Ala Thr
                  5
<210> 8
<211> 20
<212> PRT
<213> T-cell epitope HBVnc
<400> 8
Pro His His Thr Ala Leu Arg Gln Ala Ile Leu Cys Trp Gly Glu Leu
```

Met Thr Leu Ala

```
<210> 9
<211> 15
<212> PRT
<213> T-cell epitope HBsAg
<400> 9
Phe Phe Leu Leu Thr Arg Ile Leu Thr Ile Pro Gln Ser Leu Asp
                  5
<210> 10
<211> 16
<212> PRT
<213> T-cell epitope MT
<400> 10
Tyr Ser Gly Pro Leu Lys Ala Glu Ile Ala Gln Arg Leu Glu Asp Val
<210> 11
<211> 20
<212> PRT
<213> T-cell epitope HSP70
Gln Pro Ser Val Gln Ile Gln Val Tyr Gln Gly Glu Arg Glu Ile Ala
                                      10
Ser His Asn Lys
<210> 12
<211> 8
<212> PRT
<213> T-cell epitope Flag peptide
Met Asp Tyr Lys Asp Asp Asp
  1
<210> 13
<211> 657
<212> DNA
<213> Recombinant N10 construct
<220>
<221> CDS
<222> (1)..(657)
```

•			
		at cat ggt atg gct agc atg gat Is His Gly Met Ala Ser Met Asp 10 15	48
	Asp Ile Glu Gl	gt cgc aaa ggt gtt tcc atc gac Ly Arg Lys Gly Val Ser Ile Asp 25 30	96
	_	ac ccg aaa aaa ggt ctg aaa ttc sn Pro Lys Lys Gly Leu Lys Phe 45	144
		ac gaa atc gac tcc aaa ggt atc sn Glu Ile Asp Ser Lys Gly Ile 60	192
		aa ctg gac cgt tgc aac aac aaa vs Leu Asp Arg Cys Asn Asn Lys 75 80	240
		aa aaa gct tct tct gtt ttc aac Lu Lys Ala Ser Ser Val Phe Asn 90 95	288
-		ac ttc acc gtt tcc ttc tgg ctg sn Phe Thr Val Ser Phe Trp Leu 05 110	336
		ac ctg gaa aaa ggt cag tac atc is Leu Glu Lys Gly Gln Tyr Ile 125	384
		cc acc gaa aaa ggt gga tct ccg Le Thr Glu Lys Gly Gly Ser Pro 140	432
-		t ctg tgc tgg ggc gaa ctg atg Le Leu Cys Trp Gly Glu Leu Met 155 160	480
	_	at gtg aaa cag aac acc ctg aaa or Val Lys Gln Asn Thr Leu Lys 170 175	528
	_	eg ctg acc cgc att ctg acc att eu Leu Thr Arg Ile Leu Thr Ile 190	576
		et ggc ccg ctg aaa gcg gaa att er Gly Pro Leu Lys Ala Glu Ile 205	624
gcg cag cgc ctg gaa	gat gtg aaa gg	ga tcc taa	657

Ala Gln Arg Leu Glu Asp Val Lys Gly Ser 210 215

<210> 14

<211> 218

<212> PRT

<213> Recombinant N10 construct

<400> 14

Met Gly Gly Ser His His His His His Gly Met Ala Ser Met Asp 1 5 10 15

Tyr Lys Asp Asp Asp Ile Glu Gly Arg Lys Gly Val Ser Ile Asp 20 25 30

Lys Phe Arg Ile Phe Cys Lys Ala Asn Pro Lys Lys Gly Leu Lys Phe 35 40 45

Ile Ile Lys Arg Tyr Thr Pro Asn Asn Glu Ile Asp Ser Lys Gly Ile
50 55 60

Arg Glu Asp Asn Asn Ile Thr Leu Lys Leu Asp Arg Cys Asn Asn Lys
65 70 75 80

Gly Glu Lys Lys Ile Ala Lys Met Glu Lys Ala Ser Ser Val Phe Asn 85 90 95

Val Val Asn Ser Lys Gly Phe Asn Asn Phe Thr Val Ser Phe Trp Leu 100 105 110

Arg Val Pro Lys Val Ser Ala Ser His Leu Glu Lys Gly Gln Tyr Ile 115 120 125

Lys Ala Asn Ser Lys Phe Ile Gly Ile Thr Glu Lys Gly Gly Ser Pro 130 135 140

His His Thr Ala Leu Arg Gln Ala Ile Leu Cys Trp Gly Glu Leu Met 145 150 155 160

Thr Leu Ala Lys Gly Ser Pro Lys Tyr Val Lys Gln Asn Thr Leu Lys 165 170 175

Leu Ala Thr Lys Gly Ser Phe Phe Leu Leu Thr Arg Ile Leu Thr Ile 180 185 190

Pro Gln Ser Leu Asp Lys Gly Tyr Ser Gly Pro Leu Lys Ala Glu Ile 195 200 205

Ala Gln Arg Leu Glu Asp Val Lys Gly Ser 210 215

<210> 15

<212> DNA <213> Recombinant N6 construct <220> <221> CDS <222> (1) .. (432) <400> 15 atg ggg ggt tot cat cat cat cat cat ggt atg got agc atg gat 48 Met Gly Gly Ser His His His His His Gly Met Ala Ser Met Asp tac aag gac gac gat gat atc gaa ggt cgc aaa ggt gtt tcc atc gac 96 Tyr Lys Asp Asp Asp Ile Glu Gly Arg Lys Gly Val Ser Ile Asp 25 aaa ttc cqt atc ttc tqc aaa qct aac ccq aaa aaa qqt ctq aaa ttc 144 Lys Phe Arg Ile Phe Cys Lys Ala Asn Pro Lys Lys Gly Leu Lys Phe 35 40 atc atc aaa cgt tac acc ccg aac aac gaa atc gac tcc aaa ggt atc 192 Ile Ile Lys Arg Tyr Thr Pro Asn Asn Glu Ile Asp Ser Lys Gly Ile 50 55 cgt gaa gac aac aac acc ctg aaa ctg gac cgt tgc aac aac aaa 240 Arg Glu Asp Asn Asn Ile Thr Leu Lys Leu Asp Arg Cys Asn Asn Lys 65 ggt gaa aag aag atc gct aaa atg gaa aaa gct tct tct gtt ttc aac 288 Gly Glu Lys Lys Ile Ala Lys Met Glu Lys Ala Ser Ser Val Phe Asn gtt gtt aac tct aaa ggt ttc aac aac ttc acc gtt tcc ttc tgg ctg 336 Val Val Asn Ser Lys Gly Phe Asn Asn Phe Thr Val Ser Phe Trp Leu 100 105 cgt gtt ccg aaa gtt tcc gct tcc cac ctg gaa aaa ggt cag tac atc 384 Arg Val Pro Lys Val Ser Ala Ser His Leu Glu Lys Gly Gln Tyr Ile 115 120 aaa gct aac tcc aaa ttc atc ggt atc acc gaa aaa ggt gga tcc taa 432 Lys Ala Asn Ser Lys Phe Ile Gly Ile Thr Glu Lys Gly Gly Ser 130 135 <210> 16 <211> 143 <212> PRT <213> Recombinant N6 construct <400> 16 Met Gly Gly Ser His His His His His Gly Met Ala Ser Met Asp 10

<211> 432

Tyr	ьys	Asp	20	Asp	Asp	11e	GIU	25	Arg	гуѕ	GIY	vai	30	iie	Asp	
Lys	Phe	Arg 35	Ile	Phe	Cys	Lys	Ala 40	Asn	Pro	Lys	Lys	Gly 45	Leu	Lys	Phe	
Ile	Ile 50	Lys	Arg	Tyr	Thr	Pro 55	Asn	Asn	Glu	Ile	Asp 60	Ser	Lys	Gly	Ile	
Arg 65	Glu	Asp	Asn	Asn	Ile 70	Thr	Leu	Lys	Leu	Asp 75	Arg	Cys	Asn	Asn	Lys 80	
Gly	Glu	Lys	Lys	Ile 85	Ala	Lys	Met	Glu	Lys 90	Ala	Ser	Ser	Val	Phe 95	Asn	
Val	Val	Asn	Ser 100	Lys	Gly	Phe	Asn	Asn 105	Phe	Thr	Val	Ser	Phe 110	Trp	Leu	
Arg	Val	Pro 115	Lys	Val	Ser	Ala	Ser 120	His	Leu	Glu	Lys	Gly 125	Gln	Tyr	Ile	
Lys	Ala 130	Asn	Ser	Lys	Phe	Ile 135	Gly	Ile	Thr	Glu	Lys 140	Gly	Gly	Ser		
<211 <212	0> 17 l> 11 2> DN B> Re	L73 JA	oinar	nt Ni	19 co	onsti	ruct									
<220> <221> CDS <222> (1)(1173)																
)> 17											~~+	.~~		~~+	48
				cat His 5												40
				gat Asp												96
		_		ttc Phe	_		-									144
				tac Tyr												192
_	_	_		aac Asn			_		_							240

	gaa Glu													288
	gtt Val													336
	gtt Val													384
	gct Ala 130													432
	cat His													480
	ctg Leu													528
_	gcg Ala			_			_	_		_	_			576
_	cag Gln	_	_									-		624
	cag Gln 210													672
	atc Ile													720
	cgt Arg		_			-		_				_	_	768
_	aac Asn			-		_	_	_	-				_	816
_	aag Lys	_		_	_		-			_		_	_	864
	tct Ser							_			 _	_	_	912

							•									
•	290					2 9.5					300					
					tcc Ser 310											960
					ggt Gly											1008
		_	_	_	gcg Ala		-									1056
					aaa Lys											1104
					ttt Phe											1152
	ctg Leu				tcc Ser 390	taa										1173
<212 <212	<210> 18 <211> 390 <212> PRT <213> Recombinant N19 construct															
	0> 18 Gly		Ser	His 5	His	His	His	His	His 10	Gly	Met	Ala	Ser	Met 15	Asp	
Tyr	Lys	Asp	Asp 20	Asp	Asp	Ile	Glu	Gly 25	Arg	Lys	Gly	Val	Ser 30	Ile	Asp	
Lys	Phe	Arg 35	Ile	Phe	Cys	Lys	Ala 40	Asn	Pro	Lys	Lys	Gly 45	Leu	Lys	Phe	
Ile	Ile 50	Lys	Arg	Tyr	Thr	Pro 55	Asn	Asn	Glu	Ile	Asp 60	Ser	Lys	Gly	Ile	
Arg 65	Glu	Asp	Asn	Asn	Ile 70	Thr	Leu	Lys	Leu	Asp 75	Arg	Cys	Asn	Asn	Lys 80	
Gly	Glu	Lys	Lys	Ile 85	Ala	Lys	Met	Glu	Lys 90	Ala	Ser	Ser	Val	Phe 95	Asn	
Val	Val	Asn	Ser	Lys	Gly	Phe	Asn	Asn 105	Phe	Thr	Val	Ser	Phe 110	Trp	Leu	

Arg Val Pro Lys Val Ser Ala Ser His Leu Glu Lys Gly Gln Tyr Ile 115 120 Lys Ala Asn Ser Lys Phe Ile Gly Ile Thr Glu Lys Gly Gly Ser Pro 135 His His Thr Ala Leu Arg Gln Ala Ile Leu Cys Trp Gly Glu Leu Met 150 155 Thr Leu Ala Lys Gly Ser Pro Lys Tyr Val Lys Gln Asn Thr Leu Lys 165 Leu Ala Thr Lys Gly Ser Phe Phe Leu Leu Thr Arg Ile Leu Thr Ile 185 Pro Gln Ser Leu Asp Lys Gly Tyr Ser Gly Pro Leu Lys Ala Glu Ile Ala Gln Arg Leu Glu Asp Val Lys Gly Ser Val Ser Ile Asp Lys Phe 215 210 Arg Ile Phe Cys Lys Ala Asn Pro Lys Lys Gly Leu Lys Phe Ile Ile 235 230 Lys Arg Tyr Thr Pro Asn Asn Glu Ile Asp Ser Lys Gly Ile Arg Glu 245 250 Asp Asn Asn Ile Thr Leu Lys Leu Asp Arg Cys Asn Asn Lys Gly Glu 265 Lys Lys Ile Ala Lys Met Glu Lys Ala Ser Ser Val Phe Asn Val Val 280 Asn Ser Lys Gly Phe Asn Asn Phe Thr Val Ser Phe Trp Leu Arg Val 295 290 Pro Lys Val Ser Ala Ser His Leu Glu Lys Gly Gln Tyr Ile Lys Ala 310 315 Asn Ser Lys Phe Ile Gly Ile Thr Glu Lys Gly Gly Ser Pro His His 325 Thr Ala Leu Arg Gln Ala Ile Leu Cys Trp Gly Glu Leu Met Thr Leu 340 Ala Lys Gly Ser Pro Lys Tyr Val Lys Gln Asn Thr Leu Lys Leu Ala 360 Thr Lys Gly Ser Phe Phe Leu Leu Thr Arg Ile Leu Thr Ile Pro Gln 370 375 Ser Leu Asp Lys Gly Ser 385 390

<210> 19 <211> 723 <212> DNA <213> Recombinant N11 construct														
<220> <221> CDS <222> (1)(723)														
<400> 19 atg ggg ggt tct Met Gly Gly Ser 1														
tac aag gac gac Tyr Lys Asp Asp 20														
aaa ttc cgt atc Lys Phe Arg Ile 35														
atc atc aaa cgt Ile Ile Lys Arg 50	_	_	_											
cgt gaa gac aac Arg Glu Asp Asn 65		Leu Lys Leu As												
ggt gaa aag aag Gly Glu Lys Lys	-		_											
gtt gtt aac tct Val Val Asn Ser 100														
cgt gtt ccg aaa Arg Val Pro Lys 115	Val Ser Ala S													
aaa gct aac tcc Lys Ala Asn Ser 130														
cat cat acc gcg His His Thr Ala 145			s Trp Gly Glu											
acc ctg gcg aaa Thr Leu Ala Lys			s Gln Asn Thr	_										

								•							
			aaa Lys 180												576
_	_		ctg Leu	-						_	_		_		624
	_	_	ctg Leu	_	_					_	_	-	_	att Ile	672
_			cag Gln		_	_	_		_					tcc Ser 240	720
taa															723
01/															

<210> 20

<211> 240

<212> PRT

<213> Recombinant N11 construct

<400> 20

Met Gly Gly Ser His His His His His Gly Met Ala Ser Met Asp 1 5 10 15

Tyr Lys Asp Asp Asp Ile Glu Gly Arg Lys Gly Val Ser Ile Asp 20 25 30

Lys Phe Arg Ile Phe Cys Lys Ala Asn Pro Lys Lys Gly Leu Lys Phe 35 40 45

Ile Ile Lys Arg Tyr Thr Pro Asn Asn Glu Ile Asp Ser Lys Gly Ile
50 55 60

Arg Glu Asp Asn Asn Ile Thr Leu Lys Leu Asp Arg Cys Asn Asn Lys 65 70 75 80

Gly Glu Lys Lys Ile Ala Lys Met Glu Lys Ala Ser Ser Val Phe Asn 85 90 95

Val Val Asn Ser Lys Gly Phe Asn Asn Phe Thr Val Ser Phe Trp Leu 100 105 110

Arg Val Pro Lys Val Ser Ala Ser His Leu Glu Lys Gly Gln Tyr Ile 115 120 125

Lys Ala Asn Ser Lys Phe Ile Gly Ile Thr Glu Lys Gly Gly Ser Pro 130 135 140

His His Thr Ala Leu Arg Gln Ala Ile Leu Cys Trp Gly Glu Leu Met

145					150	•				155					160
Thr	Leu	Ala	Lys	Gly 165	Ser	Pro	Lys	Tyr	Val 170	Lys	Gln	Asn	Thr	Leu 175	Lys
Leu	Ala	Thr	Lys 180	Gly	Ser	Phe	Phe	Leu 185	Leu	Thr	Arg	Ile	Leu 190	Thr	Ile
Pro	Gln	Ser 195	Leu	Asp	Lys	Gly	Tyr 200	Ser	Gly	Pro	Leu	Lys 205	Ala	Glu	Ile
Ala	Gln 210	Arg	Leu	Glu	Asp	Val 215	Lys	Gly	Ser	Gln	Pro 220	Ser	Val	Gln	Ile
Gln 225	Val	Tyr	Gln	Gly	Glu 230	Arg	Glu	Ile	Ala	Ser 235	His	Asn	Lys	Gly	Ser 240